Origins of. . .

Fine needle aspiration cytology

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The use of needle aspiration for purposes of diagnosis can be traced back to 1847 when Kun described a "new instrument for the diagnosis of tumours". There followed occasional sporadic reports of this technique towards the end of the 19th century. In 1883 Leydon used needle aspiration to obtain cells to isolate pneumonic microorganisms, and three years later Menetrier used the technique to diagnose pulmonary carcinoma. In 1904 Griegg and Gray diagnosed trypanosomiasis in lymph node aspirates from patients with sleeping sickness.[1] Few pathologists were involved in this pioneering work, which was promulgated to a large extent by clinicians who used these techniques as aids to rapid diagnosis.

The first real ideological and practical impetus to aspiration cytopathology came during the interwar period. In the United Kingdom in 1927 Dudgeon and Patrick proposed needle aspiration of tumours as a means of rapid microscopic diagnosis.[2] This idea was taken on with full avidity in the early 1930s by Hayes E Martin, a head and neck surgeon, and Edward B Ellis, a chief histotechnologist at New York's Memorial Hospital for Cancer and Allied Diseases (the present Memorial Sloan-Kettering Cancer Center).[3] Much of the credit for their success deservedly goes to Fred W Stewart, the surgical pathologist responsible for interpreting the smears. In 1933 Stewart described the experience of the Memorial Hospital comprising 2500 tumours analysed by the aspiration method.[4] In his report he emphasised certain points that must be considered for optimal results:

- emphasis on the technique of aspiration and preparation of the sample;
- the importance of correlating clinical information with interpretation of the aspirated material;
- the pathologist is encouraged to compare the "picture" of the smear with conventional histology;
- for correct interpretation, the pattern of the smear must be taken into account along with detailed individual cytological features;
- and the usefulness of this method is documented for tumour diagnosis, but attention is also directed towards its limitations.

Today, more than 60 years on, these points still form the core of knowledge that must be acquired to ensure the correct and successful application of needle aspiration cytology.

The technique prospered at Memorial Hospital during the 30 years of collaboration between Martin and Stewart. However, even during this period of enthusiasm, limited interest was shown by other cancer centres in the United States. At Memorial, needle aspiration cytology was promoted as a safe alternative to open biopsy that clinicians (including Ewing, the director of pathology at the time) feared would increase the risk of tumour spread. However, as the clinicians' fears were laid to rest, the popularity of needle aspiration cytology waned to such an extent that by the 1960s the technique was all but obsolete at the Memorial.[5,6] The procedure was resurrected in the mid 1950s by Europeans. Soderstrom and Franzen in Sweden[7] and Lopes-Cardozo in Holland (all haematologists by training) became major proponents, studying thousands of cases each year. In contrast to Martin and Ellis who used thicker calibre (18 gauge) needles, the European workers popularised the technique employing thin needles (22 gauge and higher) with an external diameter of 0.6 mm or less. This is the technique used today and is known as fine needle aspiration (FNA) cytology. It was probably Mannheim in Berlin who inspired FNA following a series he reported in 1931 in which he used a 1.0 mm diameter needle.

Joseph Zajicek, among the first of pathologists to embrace FNA, in collaboration with Sixten Franzen and Torsten Lowhagen at the Radiumhemmet of the Karolinska Hospital in Sweden, applied the requisite scientific rigour to define precise diagnostic criteria in a variety of conditions. They have emphasised the simplicity, safety, rapidity and diagnostic accuracy of the technique by presenting their findings with full clinical, histological, and follow up data.[8] By operating a direct referral, clinic based service run by specialists in cytopathology who take, prepare, and interpret the aspirates, they have provided a model for FNA services for the rest of the world. Indeed, by the 1970s the Swedish experience led to a modest resurgence of interest in the technique, spread by dedicated enthusiasts to the UK, the Americas, Japan, and Australia, such that it is now part of the service of all sophisticated pathology departments. The present day focus of FNA cytology is on obtaining a satisfactory specimen on which a reliable diagnosis can be made and, therefore, that the aspirate sample should provide a true reflection of the disease

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Accepted for publication 22 January 1997

process in the patient. For this reason, FNA cytology is most useful in tumour diagnosis.

Much debate has raged over the relative merits of fine and core needles in the procurement of an aspirate sample. One feels that the use of core needles may carry a greater risk of complications than the simple fine needle of less than 21 gauge, without necessarily improving diagnostic accuracy. Core needle aspiration is an excellent tool in specific situations—for example, in the investigation of deep soft tissue tumours where an appreciation of the histological milieu is desirable. Nevertheless, rather than using it routinely, one should make efforts to improve the fine needle cytology techniques. There has been a great deal of controversy regarding the advantages and disadvantages of using air dried Romanowsky (including May-Grunwald-Giemsa (MGG)) stains compared with wet fixed Papanicolaou (Pap) preparations. In fact the two are complementary and both should be used because certain features are particularly distinctive in each. Broadly speaking, MGG yields better demonstration of cytoplasmic detail whereas Pap stain gives excellent nuclear detail. In addition haematoxylin and eosin preparations may aid in the interpretation of FNA smears. The granularity of oncocytes, and other types of granulated cells, cytoplasmic features of some endocrine cells, and the keratinisation of differentiated squamous cells are well depicted with this staining method.

Advantages of FNA

There are clear advantages of FNA to patients and doctors alike. The technique is relatively painless, produces a speedy result and is cheap. In experienced hands its accuracy can approach that of histopathology in providing definite diagnosis. The method is applicable to lesions that are easily palpable—for example, superficial growths of the skin and organs such as thyroid, breast, and superficial lymph nodes. New radiological techniques for internal imaging of organs and lesions in sites not easily accessible to surgical biopsy have opened the door for FNA of deeper impalpable structures.[9] Aspirates may be taken from the lung, prostate, and retroperitoneal organs as the first step in laboratory investigation, and can yield rapid diagnoses to satisfy eager clinicians. Costly days in hospital can be avoided as a tissue diagnosis may be obtained within minutes rather than days. This is an important consideration in today's climate of cost conscious medical care.

FNA cytology is less demanding technologically than surgical biopsy; in this respect it is eminently suitable for practice in countries with poor resources that are unable to fund teams of surgeons and nurses. The low risk of complications is an additional advantage that allows FNA cytology to be performed as an office procedure, in outpatient departments, and in radiology theatres. It is also suitable in debilitated patients, is readily repeatable, and useful for multiple lesions. However, to ensure optimal results proper training is necessary to achieve the requisite levels of expertise. We suggest that the highest standards are best attained in the setting of a busy teaching hospital centre. Ideally there should be several outpatient clinics (such as breast and neck lumps including thyroid, salivary gland, lymph node, and cysts) at which both surgeon and pathologist (with trainee) are present so that clinicopathological correlation can be achieved. It is in this environment that the trainee pathologist will have the opportunity to conduct numerous fine needle aspirates and to interpret them under the supervision of the consultant pathologist.

Limitations

FNA cytology, however, has its limitations. Sampling is scanty and histological architecture is lost thereby rendering impossible diagnoses based on histology.[3] Aspiration cytology must be used with caution in the diagnosis and classification of primary salivary gland neoplasms. For example, inflammatory, metaplastic or degenerative changes may produce sufficient atypia and pleomorphism in a benign Warthin's tumour to mimic mucoepidermoid carcinoma. Definitive treatment such as parotidectomy or neck dissection should be carried out only after histological confirmation of cytological findings.

Likewise, the use of aspiration cytology in the diagnosis of thyroid tumours is fraught with difficulty. In the case of high grade carcinomas (anaplastic, spindle cell, and giant cell) the cytological abnormalities are striking and the diagnosis relatively simple. Much more common are the orderly follicular or low grade papillary carcinomas composed of quite uniform epithelium. Aspiration cytology is indefinite in such cases and diagnosis hinges on careful histological study of multiple sections and the demonstration of invasion. In the realm of mammary lesions, FNA plays a cost effective triage role in the management of breast masses, differentiation of cysts from solid tumours, therapeutic procedures for benign cysts, and evaluation of local chest wall recurrences. The aspirated material can also be used for studies of prognostic value such as oestrogen receptor analysis and flow cytometry. In breast malignancy FNA is highly accurate when positive. Particularly difficult to diagnose, however, is lobular carcinoma. The time tested rule is that a negative cytological diagnosis is not definitive unless it is fully supported by negative clinical, radiological, and other findings. All clinically or mammographically suspicious intramammary lesions must be excised and examined histologically, without regard to a negative aspirate.[10]

Intrahepatic tumours also have been targeted by FNA. Hyperplastic liver cell nodules, liver cell adenomas, and well differentiated hepatocellular carcinomas cannot be differentiated with accuracy in the aspiration smear, thereby necessitating histology. The role of FNA in the definitive diagnosis of primary renal neoplasms is limited by the difficulty in distinguishing small hamartomatous nodules and adenomas from orderly renal carcinoma.

Furthermore renal infarction can be a potential pitfall for a false positive cytological diagnosis of malignancy.[11]

The difficulties that surround the diagnosis of malignant lymphomas from nodal aspirates cannot be overemphasised. Lymphocytes of various degrees of differentiation, often held to be the cytological indicator of benign lymphoid hyperplasia, may also be found in aspirates of lymphoma. Malignant cells of the vast majority of lymphomas are indistinguishable from benign lymphoid cells on cytological, cytochemical, and immunological grounds.

Complications

There is a risk of complications of FNA, albeit low. The overall morbidity and mortality related to FNA has been estimated in several studies and the risk of death is approximately 1 in 15 000.[12] This compares favourably with the more invasive procedures that the technique replaces. Serious complications have been reported such as major haemorrhage after FNA of lung, liver, and kidney; septicaemia after prostate aspiration; bile peritonitis following needling of the liver; and acute pancreatitis resulting from pancreatic aspiration. However, such complications are very rare considering the many thousands of uncomplicated FNA procedures that have been performed in major centres where close follow up is the rule. The possibility of cancer cells being disseminated along the needle track initially caused a great deal of concern. Review of the literature shows that multiple passes, larger needles, and absence of normal parenchyma covering the lesion appear to increase the risk. There are some contraindications to deep site aspirates. Anticoagulant therapy and intrinsic bleeding problems increase the risk of bruising and haemorrhage. Under such circumstances deep site aspirates are best avoided until the bleeding abnormality is corrected. Patients known to have abnormal heart valves should be given prophylactic penicillin during any FNA. Intractable cough and poor respiratory function are absolute contraindications to transthoracic FNA, as a full blown pneumothorax in a respiratory cripple carries considerable mortality. Aspirates of unsuspected hydatid cysts carry the potential risk of anaphylactic shock resulting from rupture and is best avoided. Fine needle aspiration of phaeochromocytomas is contraindicated for fear of inducing a hypertensive crisis.

Scientific discoveries and technological advancements have ensured the continued revival of FNA. Measurements of DNA within individual cells—for example, by flow cytometry, morphometry to measure morphological differences not appreciated by subjective assessment of the microscopic image by the human eye, and sophisticated image analysis systems for pattern and individual cell recognition have fuelled that revival increasing the potential to make precise type-specific diagnoses. Furthermore, cells obtained by FNA can be manipulated in a variety of ways useful to research: for DNA analysis (for example, polymerase chain reaction), ultrastructural study, immunohistochemistry, gene rearrangement, morphometry, and image analysis.[13 14]

FNA is now established as the first line investigation of mass lesions wherever they occur in the body. It is hoped that FNA will continue to have this pride of place, but to that end the 1983 quote from Christopherson would appear to ring true: "Fine-needle aspiration for tumour diagnosis has survived for half a century and will continue to survive provided it is not overdone and is not used injudiciously."[15]

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